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Original Article

Ultrasound Elastography to Differentiate the Thrombus and Plaque in Peripheral Arterial Diseases

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Purpose: Arterial stiffness and steno-occlusion of the lower-extremity can result from many vascular lesions, including acute thromboembolisms, soft plaques, calcified plaques, or inflammatory disease. Ultrasound (US) elastography measures the tissue deformation response to compression and displays tissue stiffness. This study aimed to evaluate the characteristics of arterial lesions in the lower extremities using US elastography.

Materials and Methods: We retrospectively analyzed the data of 20 patients who visited our institute for arterial disease treatment between May 2016 and November 2017. An US examination with B-mode and strain elastography (SE) was performed of four different lesion types at 45 sites: acute and subacute thromboembolisms, soft plaques, calcified plaques, and thromboangiitis obliterans lesions (TAOs). During SE, stress was externally applied by the operator using the transducer. Strain ratio (SR) was calculated as the fraction of the average strain in the reference area divided by the average strain in the lesion. The SR was compared among different lesion types, with the accompanying vein as the reference region of interest.

Results: The strain was highest in the soft plaques (0.63%±0.23%), followed by the TAOs (0.45%±0.11%), calcified plaques (0.44%±0.13%), and acute thromboembolisms (0.34%±0.23%), which were statistically significant (P=0.026). However, the mean SR was highest for the calcified plaques (2.33%±0.80%), followed by the TAOs (1.63%±0.40%), acute thromboembolisms (1.60%±0.48%), and soft plaques (1.51±0.39), and which were statistically significant (P=0.013).

Conclusion: Despite several limitations, vascular elastography may be useful for differentiating between lesion types in peripheral arterial disease.

Key Words: Ultrasonography, Elastography, Peripheral arterial disease, Elasticity imaging techniques, Vascular stiffness

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INTRODUCTION

Peripheral arterial disease (PAD) is characterized by arterial stenosis or occlusion anywhere from the aortoiliac segment to the pedal arteries due to acute thrombosis or embolism, soft atherosclerotic plaques, calcified plaques, or inflammatory disease [1]. PAD is a serious public health problem worldwide. The incidence of lower-extremity arterial disease is approximately 1.5 cases per 10,000 people per year [2]. Stenosis or occlusion decreases limb perfusion and may present as various clinical manifestations ranging from intermittent claudication to critical limb-threatening isch-

emia (CLTI) in acute or chronic settings depending on the etiology. Acute limb ischemia (ALI) affects all metabolically active limb tissues including the skin, muscles, and nerves. [3] Complications are common among patients with ALI, and despite early revascularization, 30-day mortality and amputation rates are 10% to 15% [4,5]. In addition to ALI, CLTI also exhibits reduced life expectancy, with mortality typically exceeding 50% by 5 years [6]. Therefore, an accurate and prompt diagnosis of CLTI can help facilitate the proper treatment of these patients.

Several imaging modalities can be used to determine the location and characteristics of vascular lesions and establish treatment plans in patients with PAD, including ultrasound (US), computed tomography angiography (CTA), magnetic resonance angiography, and invasive angiography [7]. US elastography is a recently developed technique that measures tissue deformation in response to compression and reveals tissue stiffness. Stiffness increases in diseased arteries, and its degree differs among thromboembolisms, soft plaques, calcified plaques, and inflammatory disease [1]. It is important to distinguish among lesion types to ensure their appropriate treatment. Therefore, this study aimed to evaluate the strain and strain ratios (SRs) of different lower-extremity arterial lesion types.

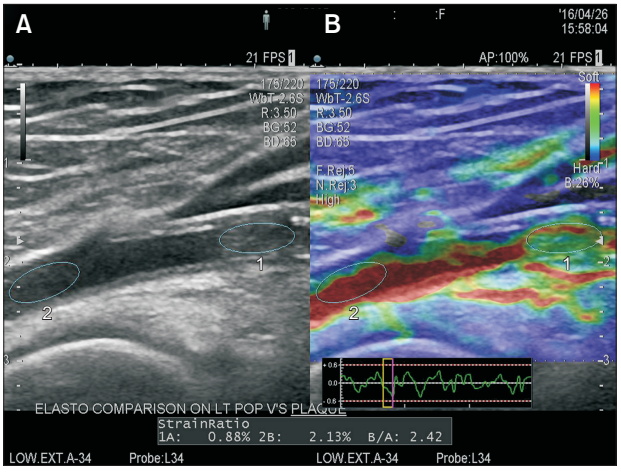

Fig. 1. Measurement of strain ratio comparing the lesion and the proximal normal segment. (A) The lesion and normal proximal segment were selected on a gray-scale image. The region of interest of the lesion (circle 1) and the proximal normal segment (circle 2) were shown. (B) After color mapping, the strains of the lesion (circle 1, 0.88%) and the proximal normal segment (circle 2, 2.13%) were measured and the strain ratio was calculated (2.42).

MATERIALS AND METHODS

1) Patients

The study included patients who visited our institute for PAD treatment. The patients included in this study had chronic total steno-occlusion, acute thrombus of chronic lesions, or a suspected embolism. Patients who did not agree to participate in this study, those who had a thromboembolism due to a malignancy, and those who had a thromboembolism due to an aneurysm were excluded. Hence, this retrospective study included a prospectively enrolled registry of 20 patients. US elastography was performed diagnostically. This study was approved by the Institutional Review Board of Kyung Hee University Hospital at Gangdong (no. 2022-08-011), and written consent was obtained from all patients.

2) Ultrasonography

B-mode US and strain elastography (SE) were performed using an E-CUBE 15 EX (Alpinion Medical Systems, Seoul, Korea) with a 3- to 12-MHz linear probe. Stress was applied externally to the transducer by the same operator. SE measures the axial tissue displacement caused by mechanical stress in real time. The strain and SR were calculated for different lesion types with proximal normal segments as the reference regions of interest (ROI). The SR was calculated as the fraction of the average strain in the reference area divided by the average strain in the lesion (Fig. 1).

If the proximal normal segment could not be used as reference, SR was calculated using the accompanying vein

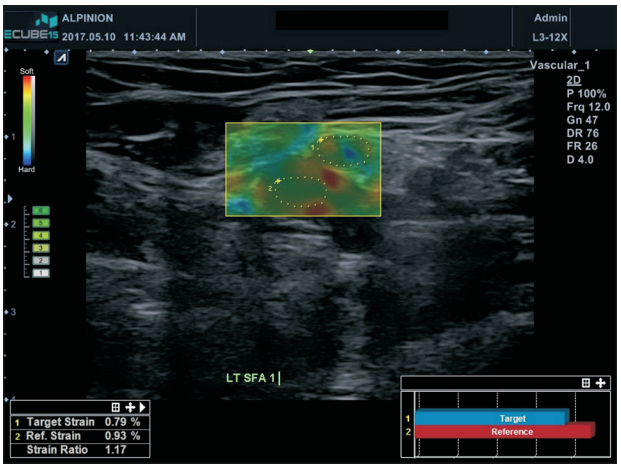

Fig. 2. Measurement of strain ratio comparing the lesion and the adjacent vein. Yellow dotted circles 1 and 2 indicate the region of interest of the lesion and the adjacent vein, respectively. The strain ratio was calculated as 1.17.

as the reference ROI. The SRs of different lesion types were compared using the accompanying vein as the reference ROI (Fig. 2).

The lesions were classified into acute thromboembolisms, soft plaques, calcified plaques, and thromboangiitis obliterans lesions (TAOs) on axial and maximal-intensity projection images from preoperative CT or angiography. Lesion type was confirmed by evaluation of a surgical specimen's gross appearance and hardness. Acute thromboembolism samples were obtained via conventional open thromboembolectomy using an embolectomy catheter. Soft plaques were obtained via percutaneous directional atherectomy using a Silverhawk or Turbohawk catheter (Medtronic Inc., Minneapolis, MN, USA). An acute thrombus and soft plaque are shown in Fig. 3. Calcified plaques were confirmed using preoperative CTA and examination of the obtained specimen. On the preoperative non-contrast CTA images, the calcified plaque demonstrated high intensity. Calcified plaques were detected by evaluation of the specimen after percutaneous atherectomy.

One-way analysis of variance was used to perform the statistical analysis. The significance level was set at $P<0.05$, and the statistical analysis was performed using SPSS ver-

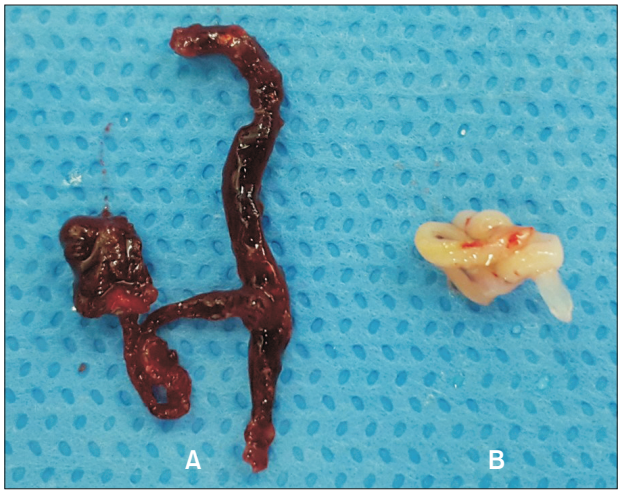

Fig. 3. Surgical specimen. Lesion types were confirmed after obtaining of the surgical specimen. (A) An acute thromboembolism was obtained using conventional open thrombectomy. (B) Soft plaques were obtained by percutaneous directional atherectomy using a Silverhawk or Turbohawk atherectomy device.

Table 1. Strain and strain ratio of each lesion

Lesion type	Strain		Strain ratio	
	Mean (%)	SD (%)	Mean (%)	SD (%)
Reference	0.85	0.39	-	-
Acute thrombus/embolus	0.34	0.23	1.60	0.48
Soft plaque	0.63	0.23	1.51	0.39
Calcified plaque	0.44	0.13	2.33	0.80
Buerger disease	0.45	0.11	1.63	0.40
P-value	0.026		0.013	

P-value was analyzed with one-way ANOVA test.
SD, standard deviation.

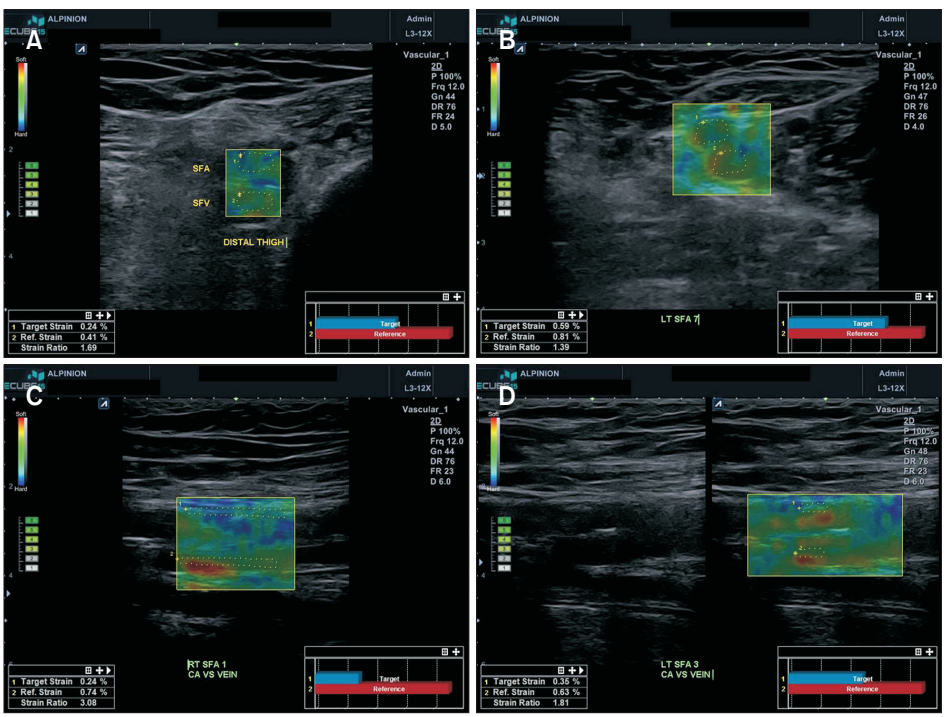

Fig. 4. Typical images demonstrated the strain ratio of each lesion type. (A) Acute thrombus (1.69), (B) soft plaque (1.39), (C) calcified plaque (3.08), (D) Buerger disease (1.81).

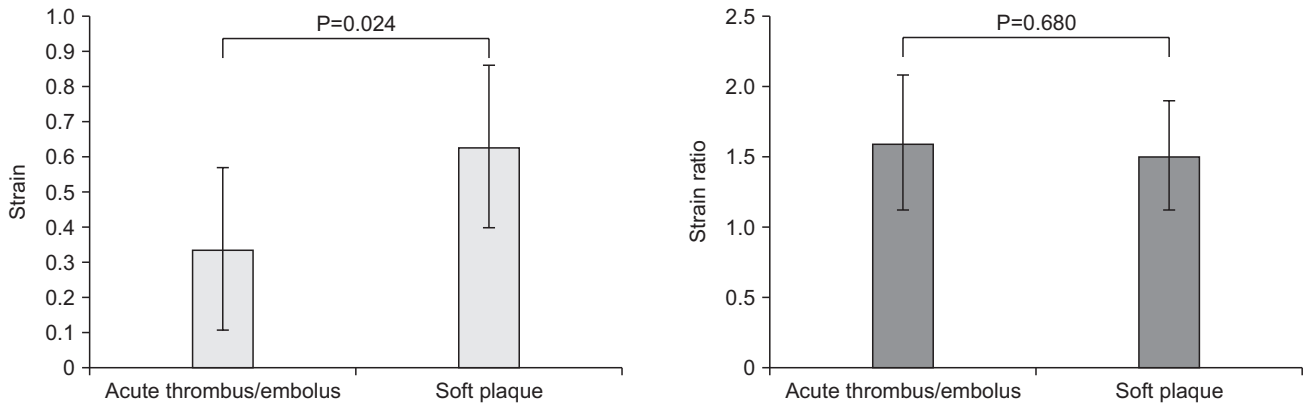

Fig. 5. Strain and strain ratio of acute thromboembolisms and soft plaques. The mean strain of the soft plaques was higher than that of the acute thromboembolisms (P=0.024). The mean strain ratio did not differ significantly between groups (P=0.680).

sion 22.0 software (IBM Corp., Armonk, NY, USA).

RESULTS

SE was performed in 45 sites. The mean±standard deviation strain of the reference ROIs was 0.85%±0.39%. For the reference ROIs, the accompanying veins were used at 40 sites (36 femoral veins, three common femoral veins, and one popliteal vein). The ROIs for the remaining five sites were used for the proximal normal arterial segments. Calculated strain for the four lesion types was highest for the soft plaques (0.63%±0.23%), followed by TAOs (0.45%±0.11%), calcified plaques (0.44%±0.13%), and acute thromboembolisms (0.34%±0.23%), differences among which were statistically significant (P=0.026). However, the mean SR was the highest for the calcified plaques (2.33%±0.80%), followed by TAOs (1.63%±0.40%), acute thromboembolisms (1.60%±0.48%), and soft plaques (1.51%±0.39%), the differences among which were statistically significant (P=0.013; Table 1). B-mode images of the lesions with a superimposed shear strain map are shown in Fig. 4. The mean strain of the soft plaques was higher than that of the acute thromboembolisms, whereas mean SR did not differ significantly between them (P=0.024 and P=0.680, respectively; Fig. 5).

DISCUSSION

PAD is among the most common manifestations of atherosclerosis. Although most patients with PAD are asymptomatic, as the disease progresses, many experience typical symptoms such as intermittent claudication, rest pain, or gangrene. CLTI accounts for 25% of deaths and 30% of major amputations annually [3]. In the treatment of PAD, lesion characteristics are associated with procedural success as well as prognosis [8]. There are multiple potential revascularization procedures, and decision-making involves consideration of the disease pattern. Heavily calcified lesions may not be treatable without debulking with atherectomy since balloons and stents alone may be unable to create an adequate lumen to facilitate adequate blood flow. Therefore, a precise evaluation of lesion type is important in the diagnosis of CLTI because it enables timely diagnosis, reduces unnecessary invasive procedures, and predicts prognosis.

US elastography was first introduced by Ophir et al. [9] in 1991. This is a non-invasive US technique that measures the degree of tissue hardness and calculates the response to compression between two points determined along the local longitudinal plane of the tissue under investigation [10]. US elastography considers changes in soft tissue elasticity in various pathologies to yield qualitative and quantitative information that can be used for diagnostic purposes [11]. Tissues can be evaluated based on their SRs and patterns. SR was obtained by dividing the hardness (strain) of the surrounding normal tissue by the degree of hardness of the affected tissue. Scoring systems that evaluate a lesion's hardness are used to estimate strain patterns [9,12-17].

US elastography was first developed to identify malignancies in breast tumors. Using US elastography, the specificity for malignancy was improved from 78% to 91.5% [18]. This method was further extended to thyroid, prostate, and liver cancer diagnoses. It is also used to diagnose cancer of the lymph nodes. The utility of US elastography in vascular disease treatment remains limited, and its application has been reported mainly in deep vein thrombosis and carotid artery disease [19]. However, considering that US is widely used for preoperative evaluations as well as during and after the treatment of vascular diseases, the potential appli-

cability of US elastography seems wide.

In the field of vascular disease, US elastography has mainly been applied in the treatment of carotid disease [20-23]. Many studies have reported its feasibility, and the accuracy of quantitative elasticity measurements is comparable to those of other diagnostic modalities [23]. In carotid disease, US elastography was used to assess plaque vulnerability and predict stroke, and vulnerable plaques had higher strain values [24,25]. However, most studies were limited to distinguishing vulnerable from non-vulnerable plaques, and no studies have yet differentiated plaques from thromboembolisms or classified plaques based on their properties. Here we compared the stiffnesses of different arterial lesions in patients with PAD and found that strain and SR differed significantly among lesion types. The mean strain was highest in soft plaques and lowest in acute thromboembolisms, while the mean SR was highest in calcified lesions. Therefore, elastography can help distinguish among lesion types and aid in appropriate treatment planning for PAD.

This study has several limitations. First, we used only one type of US machine to examine a small number of samples (45 lesions), which limits the generalizability of our findings. Second, a subgroup analysis could not be performed of variables such as age, sex, and lesion site. In addition, acute/chronic thromboembolisms were not separately classified. Mixed lesions, such as soft/calcified plaques with thrombi, were not included. The actual strain values of each lesion can be important in deciding the treatment modality. However, we could not demonstrate such values owing to the small sample size. Another limitation of this study was its lack of sensitivity, specificity, and accuracy data. However, the strength of our study is that it demonstrated the applicability of US elastography for distinguishing among different lesion types to facilitate preoperative planning. Further studies of larger cohorts are warranted to evaluate and characterize the stiffness of lower-extremity arterial lesions using US elastography.

CONCLUSION

The present study established the preliminary application of US elastography in PAD. The mean strain was the highest in soft plaques and lowest in acute thromboembolisms. Mean SR was the highest in calcified lesions, while no significant differences were noted in mean SR between acute thromboembolisms and soft plaques. Therefore, US elastography may be useful for differentiating among lesion types in patients with PAD.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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AUTHOR CONTRIBUTIONS

Concept and design: JHJ, HK. Analysis and interpretation: JHJ, HK, SC. Data collection: JHJ, HK, SC. Writing the article: KDK, HK. Critical revision of the article: SHL, HK. Final approval of the article: JHJ, KDK. Statistical analysis: SHL, HK. Overall responsibility: all authors.

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